

Applicants: Kung, *et al.*
U.S.S.N.: 10/590,672

REMARKS

Upon entry of this amendment, claims 1-11, 17, and 60-61 will be pending in the application. Claims 12 and 13 have been canceled. Claims 14-16 and 18-59 have been canceled for being drawn to non-elected invention. Claims 1 and 8 have been amended. Support for the amendments can be found throughout the specification as-filed, *e.g.*, at least in original claim 13; at page 12, lines 14-16, and at Examples 17 and 18 of the specification. New claims 60 and 61 have been added. Support for the new claims can be found at least in original claim 13. Thus, no new matter is added.

Information Disclosure Statement

Applicants acknowledge with appreciation that the Examiner has considered the information disclosure statement submitted on May 26, 2009. However, Applicants note that the Examiner did not initial cited references A1 and A2, corresponding to U.S. Patent Nos. 4,987,071 and 5,116,742. Applicants request that the Examiner initial cited references A1 and A2 and include a copy of the initialed modified Form 1449/PTO with the next communication to Applicants.

Objections to the Specification

The Examiner has objected to the specification because it contains an embedded hyperlink. *See*, Office Action at page 3. The specification has been amended to delete the hyperlink, as requested by the Examiner. This objection should be withdrawn.

The Examiner has objected to the specification because of the use of improperly demarcated trademarks. *See*, Office Action at page 3. The specification has been amended to properly demarcate trademarks. This objection should be withdrawn.

Claim Rejections -- 35 U.S.C. § 112, second paragraph

Claim 8 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for insufficient antecedent basis. *See*, Office Action at page 3. Claim 8 has been amended herein to depend from claim 7, which contains the proper antecedent basis for claim 8. This rejection should be reconsidered and withdrawn.

Applicants: Kung, *et al.*
U.S.S.N.: 10/590,672

Claim Rejections -- 35 U.S.C. § 102(b)

Claims 1-9, 11-12, and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,337,338 to Kozlowski (“Kozlowski”), as evidenced by U.S. Publication No. US 2005-0075358 A1 to Carboni (“Carboni”), and Doxorubicin Proposed PI Update. *See*, Office Action at page 4.

Claim 1, from which the remaining claims subject to the rejection depend, has been amended herein to incorporate the limitations of claim 13, which the Examiner has acknowledged is patentable over the cited art. Thus, Applicants submit that claim 1, and those dependent therefrom, is not anticipated by Kozlowski, and that this rejection should be reconsidered and withdrawn.

Claims 1, 7, 10-13, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by WO/2002/092599 to Capraro (“Capraro”) as evidenced by Carboni. *See*, Office Action at page 7. According to the Examiner, Capraro describes a method of inhibiting tumor cell growth comprising administering a composition comprising an IGF-1R inhibitor, NVP-AEW541, or its analogs. *See*, Office Action at page 8.

As stated above, claim 1, from which the remaining claims subject to the rejection depend, has been amended herein to recite a method of inhibiting multiple myeloma cell growth in a subject by administering to the subject a cytotoxic or a chemotherapeutic agent and a composition comprising an IGF-1R inhibitor, wherein the IGF-1R inhibitor is ADW-742 or NVP-AEW541.

Applicants submit that Capraro does not describe or suggest methods of inhibiting multiple myeloma cell growth, as required by the amended claims. Thus, Applicants submit that claim 1, and those dependent therefrom, is not anticipated by Capraro, and that this rejection should be reconsidered and withdrawn.

Claims 1, 2, 7, 12, and 17 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Publication No. US 2004/0072760 to Carboni (“Carboni II”) as evidenced by U.S. Publication No. US 2004/0044203 to Wittman (“Wittman”). *See*, Office Action at page 10.

Claim 1, from which the remaining claims subject to the rejection depend, has been amended herein to incorporate the limitations of claim 13, which the Examiner has

Applicants: Kung, *et al.*
U.S.S.N.: 10/590,672

acknowledged is patentable over the cited art. Thus, Applicants submit that claim 1, and those dependent therefrom, is not anticipated by Carboni II, and that this rejection should be reconsidered and withdrawn.

Claim Rejections -- 35 U.S.C. § 103(a)

Claims 1-13, and 17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kozlowski in view of Capraro as evidenced by Carboni, and by Doxorubicin Proposed PI Update. *See*, Office Action at page 11.

According to the Examiner, Kozlowski describes a method of inhibiting tumor cell growth by administering an IGF-1R inhibitor; however, Kozlowski does not describe the small molecule tyrosine kinase, NVP-AEW541. The Examiner also states that Capraro describes a method of inhibiting tumor cell growth by administering NVP-AEW541. The Examiner concludes that it would have been *prima facie* obvious for one skilled in the art to replace the IGF-1R inhibitor of Kozlowski with the NVP-AEW541 of Capraro to inhibit IGF-1R-dependent tumor cell growth. *See*, Office Action at page 12.

Claim 1, from which the remaining claims subject to the rejection depend, has been amended herein to recite a method of inhibiting multiple myeloma cell growth in a subject by administering to the subject a cytotoxic or a chemotherapeutic agent and a composition comprising an IGF-1R inhibitor, wherein the IGF-1R inhibitor is ADW-742 or NVP-AEW541.

Applicants submit that Kozlowski does not describe or suggest methods of inhibiting multiple myeloma cell growth, as required by claim 1. Capraro does not cure the deficiencies of Kozlowski, as Capraro also fails to describe or suggest methods of inhibiting multiple myeloma cell growth. Thus, Applicants submit that claim 1, from which the remaining claims depend, is not obvious in view of Kozlowski and Capraro, and that this rejection should be reconsidered and withdrawn.

Claims 1-10, 12-13, and 17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kozlowski in view of Capraro and U.S. Patent No. 6,692,742 to Nakamura (“Nakamura”). *See*, Office Action at pages 13-14.

According to the Examiner, Kozlowski describes a method of inhibiting tumor cell growth by administering an IGF-1R inhibitor, and Capraro describes a method of inhibiting tumor cell growth by administering NVP-AEW541; however, Capraro does not describe the sub-

Applicants: Kung, *et al.*

U.S.S.N.: 10/590,672

therapeutic dose for melphalan. The Examiner states that Nakamura describes a cancer therapy method comprising administering an anti-cancer antibody and melphalan, and that melphalan does not achieve a therapeutic benefit at 1 mg/kg, when administered alone. The Examiner concludes that it would have been *prima facie* obvious for one skilled in the art to inhibit a tumor growth by administering NVP-AEW541, along with a sub-therapeutic dose of melphalan. *See*, Office Action at pages 14-15.

As stated above, claim 1, from which the remaining claims subject to the rejection depend, has been amended herein to recite a method of inhibiting multiple myeloma cell growth in a subject by administering to the subject a cytotoxic or a chemotherapeutic agent and a composition comprising an IGF-1R inhibitor, wherein the IGF-1R inhibitor is ADW-742 or NVP-AEW541.

As stated above, Kozlowski does not describe or suggest methods of inhibiting multiple myeloma cell growth, as required by the claims. Secondary reference, Capraro does not cure the deficiencies of Kozlowski, as Capraro also fails to describe or suggest methods of inhibiting multiple myeloma cell growth.

Secondary reference, Nakamura, does not cure the deficiencies of Kozlowski and Capraro, as Nakamura also does not describe or suggest a method of inhibiting multiple myeloma cell growth in a subject by administering to the subject a cytotoxic or a chemotherapeutic agent and a composition comprising an IGF-1R inhibitor, wherein the IGF-1R inhibitor is ADW-742 or NVP-AEW541, as required by claim 1. Nakamura is merely cited for the proposition that melphalan could produce a therapeutic effect when administered in combination with another anti-cancer agent.

Applicants respectfully submit that the ordinary skilled artisan would not have been motivated to combine the teachings of Kozlowski and Capraro with those of Nakamura to reach the claimed invention with predictable results. Even if the skilled artisan were to rely on Kozlowski and Capraro for describing a method of inhibiting tumor cell growth by administering an IGF-1R inhibitor, NVP-AEW541, he would not have been motivated to combine the teachings with those of Nakamura to arrive at the claimed methods of inhibiting multiple myeloma growth by administering ADW-742 or NVP-AEW541, as Nakamura does not even mention the administration of an IGF-1R inhibitor (and certainly not ADW-742 or NVP-AEW541), along with a cytotoxic or chemotherapeutic agent for inhibiting tumor cell growth.

Applicants: Kung, *et al.*
U.S.S.N.: 10/590,672

Rather, Nakamura merely describes the administration of a nitrogen mustard anticancer agent and an anti-IL-6 receptor antibody.

Thus, Applicants submit that claim 1, from which the remaining claims depend, is not obvious in view of Kozlowski, Capraro, and Nakamura, and that this rejection should be reconsidered and withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants submit the pending claims are in condition for allowance. Such action is respectfully requested. The Commissioner is authorized to charge any fees that may be due to Deposit Account No. 50-0311, Reference No. 20363-025 NATL.

Respectfully submitted,

/Cynthia A. Kozakiewicz/
Ivor R. Elrifi, Reg. No. 39,529
Cynthia A. Kozakiewicz, Reg. No. 42,764
Attorneys for Applicants
c/o MINTZ, LEVIN.
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

Date: August 31, 2009

4700523v.2